

# **Arboviral Infections**

**Organism:** Arthropod-borne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes, ticks, sand flies, or midges. Other modes of transmission for some arboviruses may include blood transfusion, organ transplantation, perinatal transmission, consumption of unpasteurized dairy products, breast feeding, and laboratory exposures. More than 130 arboviruses are known to cause human disease. Most arboviruses of public health importance belong to one of three virus genera: *Flavivirus*, *Alphavirus*, and *Orthobunyavirus*.

Examples include:

- [Chikungunya Fever](#)
- [Eastern Equine Encephalitis](#)
- [Heartland virus](#)
- [Japanese Encephalitis](#)
- [LaCrosse Encephalitis](#)
- [Powassan](#)
- [Saint Louis Encephalitis](#)
- [West Nile Encephalitis](#)
- [Yellow Fever](#)
- [Dengue Fever](#)

**Incubation period:** Variable depending on specific virus; generally 2-3 weeks

**Infectious period:** Usually not person-to-person

**Transmission route:** From exposure to an arthropod vector, generally, a mosquito; or infrequently, blood transfusion

**Treatment:** No specific treatment; often symptomatic treatment as needed

## **Information Needed for the Investigation**

### **Verify the Diagnosis**

- Interview the patient for potential exposures and travel history.
- There is an embedded West Nile Virus form in AK STARS, but as a start you can use the WA DOH generic arboviral form available at:  
<http://www.doh.wa.gov/Portals/1/Documents/5100/210-066-ReportForm-Arbovirus.pdf>
- There is a specific Dengue Fever Form available at:  
[http://www.cdc.gov/dengue/resources/dengueCaseReports/DCIF\\_English.pdf](http://www.cdc.gov/dengue/resources/dengueCaseReports/DCIF_English.pdf)
- Ensure that correct tests have been ordered; consult CDC as appropriate.

### **Case definitions**

- Available on CDC's website: <http://wwwn.cdc.gov/nndss/script/casedefDefault.aspx> (arboviral diseases; dengue)

## **Clinical Description**

Most arboviral infections are asymptomatic. Clinical disease ranges from mild febrile illness to severe encephalitis. For the purpose of surveillance and reporting, based on their clinical presentation, arboviral disease cases are often categorized into two primary groups: neuroinvasive disease and nonneuroinvasive disease.

### Neuroinvasive disease

Many arboviruses cause neuroinvasive disease such as aseptic meningitis, encephalitis, or acute flaccid paralysis (AFP). These illnesses are usually characterized by the acute onset of fever with headache, myalgia, stiff neck, altered mental status, seizures, limb weakness, or cerebrospinal fluid (CSF) pleocytosis. AFP may result from anterior ("polio") myelitis, peripheral neuritis, or post-infectious peripheral demyelinating neuropathy (i.e., Guillain-Barré syndrome). Less common neurological manifestations, such as cranial nerve palsies, also occur.

### Non-neuroinvasive disease

Most arboviruses are capable of causing an acute systemic febrile illness (e.g., West Nile fever) that may include headache, myalgias, arthralgia, rash, or gastrointestinal symptoms. Some viruses also can cause more characteristic clinical manifestations, such as severe polyarthralgia or arthritis due to Chikungunya virus or other alphaviruses (e.g., Mayaro, Ross River, O'nyong-nyong).

A clinically compatible case of arboviral disease is as defined as follows:

#### Neuroinvasive disease

- Meningitis, encephalitis, acute flaccid paralysis, or other acute signs of central or peripheral neurologic dysfunction, as documented by a physician, AND
- Absence of a more likely clinical explanation. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis and/ or nuchal rigidity.

#### Non-neuroinvasive disease

- Fever (chills) as reported by the patient or a health-care provider, AND
- Absence of neuroinvasive disease, AND
- Absence of a more likely clinical explanation. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis and/ or nuchal rigidity.

## **Laboratory Criteria for Diagnosis**

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF or serum.

*Note that Dengue Fever is more complicated; consult laboratory and case definition specific for this virus: <http://www.cdc.gov/dengue/clinicalLab/laboratory.html>*

## **Case Classification**

### **Probable**

#### Neuroinvasive disease

A case that meets the above clinical criteria for neuroinvasive disease and the following laboratory criteria:

- Virus-specific IgM antibodies in CSF or serum but with no other testing.

#### Non-neuroinvasive disease

A case that meets the above clinical criteria for non-neuroinvasive disease and the laboratory criteria for a probable case:

- Virus-specific IgM antibodies in serum but with no other testing.

### **Confirmed**

#### Neuroinvasive disease

A case that meets the above clinical criteria for neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF, with or without a reported pleocytosis, and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.

#### Non-neuroinvasive disease

A case that meets the above clinical criteria for non-neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, or other body fluid, excluding CSF, OR
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen.

*Note that Dengue Fever varies somewhat from this definition; consult the more specific case definition specific for this virus: <http://wwwn.cdc.gov/nndss/script/casedefDefault.aspx>*

## Determine the Extent of Illness

- If exposure is suspected to be local (i.e., no travel history), we will need to consult CDC and discuss potential unusual sources of virus and/or changes in vector population.
- Depending on the travel history, information may need to be relayed back to the state/jurisdiction where the exposure occurred.

## Laboratory Specimens

Laboratory testing will be generally by a commercial lab; there is no capacity at ASVL to process these specimens. For unique situations, contact CDC to see about specific testing capacity: CDC Fort Collins, [dvbd@cdc.gov](mailto:dvbd@cdc.gov), (970) 221-6400.

- General CDC info about specimen submission: <http://www.cdc.gov/ncezid/dvbd/specimensub/index.html>
- For Dengue, specimens can be routed via ASPHL or ASVL to CDC Fort Collins for testing (no longer sent to Puerto Rico).
- Fillable test request form: <http://www.cdc.gov/laboratory/specimen-submission/pdf/form-50-34.pdf>.
- Recommend clinician consult with CDC/experts if they are looking for specific details on interpreting diagnostics or patient status.

## Hospital Considerations

### Contact and Control Measures

- None indicated.
- Some of these cases have caused media inquiries and community concern; consider the need for educational materials.

## Reporting Requirements

- FTR: write up cluster investigations
- AK STARS: enter all *confirmed* and *probable* cases. Select “Arboviral diseases” as the disease, then choose the appropriate virus as the Secondary Condition. Please ensure that cases with travel history are marked as “imported” in AK STARS. For “Dengue”, select “Dengue virus” as its own Primary Disease category.
- CDC cannot process reports sent through weekly NETSS transmissions and requires reporting via ArboNet: <https://wwwn.cdc.gov/arboNet/login.aspx>. Data for ArboNet can be coded to “statewide” as opposed to the specific residence borough/region of each case. Alaska cases are likely to all be imported for the foreseeable future and in allowing data to be mapped, consider whether specifying the residence may be too revealing for an individual case.

## Resources

- USGS Arboviral disease maps: <http://diseasemaps.usgs.gov/index.html>
- CDC/DVBD: <http://www.cdc.gov/ncezid/dvbd/about.html>

### **Other CDC Notes:**

In June 2014, the Council of State and Territorial Epidemiologists (CSTE) recommended Chikungunya virus become nationally notifiable. Chikungunya virus will be added to the list of National Notifiable Infectious Conditions when the CDC receives Office of Management and Budget (OMB) Paperwork Reduction Act (PRA) approval to receive data for this condition.

### Imported arboviral diseases

Human disease cases due to Dengue or Yellow fever viruses are nationally notifiable to CDC using specific case definitions. However, many other exotic arboviruses (e.g., Chikungunya, Japanese encephalitis, Tick-borne encephalitis, Venezuelan equine encephalitis, and Rift Valley fever viruses) are important public health risks for the United States as competent vectors exist that could allow for sustained transmission upon establishment of imported arboviral pathogens. Health care providers and public health officials should maintain a high index of clinical suspicion for cases of potentially exotic or unusual arboviral etiology, particularly in international travelers. If a suspected case occurs, it should be reported to the appropriate local/state health agencies and CDC.

### Interpreting arboviral laboratory results:

- **Serologic cross-reactivity:** In some instances, arboviruses from the same genus produce cross-reactive antibodies. In geographic areas where two or more closely-related arboviruses occur, serologic testing for more than one virus may be needed and results compared to determine the specific causative virus. For example, such testing might be needed to distinguish antibodies resulting from infections within genera, e.g., flaviviruses such as West Nile, St. Louis encephalitis, Powassan, Dengue, or Japanese encephalitis viruses.
- **Rise and fall of IgM antibodies:** For most arboviral infections, IgM antibodies are generally first detectable at 3 to 8 days after onset of illness and persist for 30 to 90 days, but longer persistence has been documented (e.g., up to 500 days for West Nile virus). Serum collected within 8 days of illness onset may not have detectable IgM and testing should be repeated on a convalescent-phase sample to rule out arboviral infection in those with a compatible clinical syndrome.
- **Persistence of IgM antibodies:** Arboviral IgM antibodies may be detected in some patients months or years after their acute infection. Therefore, the presence of these virus-specific IgM antibodies may signify a past infection and be unrelated to the current acute illness. Finding virus-specific IgM antibodies in CSF or a fourfold or greater change in virus-specific antibody titers between acute- and convalescent-phase serum specimens provides additional laboratory evidence that the arbovirus was the likely cause of the patient's recent illness. Clinical and epidemiologic history also should be carefully considered.
- **Persistence of IgG and neutralizing antibodies:** Arboviral IgG and neutralizing antibodies can persist for many years following a symptomatic or asymptomatic infection. Therefore, the presence of these antibodies alone is only evidence of previous infection and clinically compatible cases with the presence of IgG, but not IgM, should be evaluated for other etiologic agents.
- **Arboviral serologic assays:** Assays for the detection of IgM and IgG antibodies commonly include enzyme-linked immunosorbent assay (ELISA), microsphere immunoassay (MIA), or immunofluorescence assay (IFA). These assays provide a presumptive diagnosis and should have confirmatory testing performed. Confirmatory testing involves the detection of

arboviral-specific neutralizing antibodies utilizing assays such as plaque reduction neutralization test (PRNT).

- **Other information to consider.** Vaccination history, detailed travel history, date of onset of symptoms, and knowledge of potentially cross-reactive arboviruses known to circulate in the geographic area should be considered when interpreting results.